

no changes in sensorimotor abilities were detected by using the open field activity test (data not shown).

Example 20

[0149] It has been discovered using cultured cortical neurons that cotinine inhibits A β oligomerization in vitro and prevents its toxicity on cortical neurons. Studies performed in vitro have shown that cotinine binds to A β with high affinity. Cotinine can also bind A β in vivo with high affinity and consequently, when labeled for detection by Positron Emission tomography, it can be used as a diagnostic tool to determine the presence of senile plaques in the brain of AD patients.

[0150] It should be understood that the examples and embodiments described herein are for illustrative purposes only and that various modifications or changes in light thereof will be suggested to persons skilled in the art and are to be included within the spirit and purview of this application and the scope of the appended claims. In addition, any elements or limitations of any invention or embodiment thereof disclosed herein can be combined with any and/or all other elements or limitations (individually or in any combination) or any other invention or embodiment thereof disclosed herein, and all such combinations are contemplated with the scope of the invention without limitation thereto.

REFERENCES

- [0151] U.S. Pat. No. 4,938,949
- [0152] Berendsen H J C, van der Spoel, D., and van Drunen, D (1995) GROMACS: A message-passing parallel molecular dynamics implementation. *Computer Physics Communications* 91, 43-56.
- [0153] Birtwistle J, Hall K (1996) Does nicotine have beneficial effects in the treatment of certain diseases? *Br J Nurs* 5, 1195-1202.
- [0154] Boscarino, J E (2006). Posttraumatic stress disorder and mortality among U.S. Army veterans 30 years after military service. *Ann Epidemiol* 16 (4)248-56.
- [0155] Brewer G J (1995) Serum-free B27/neurobasal medium supports differentiated growth of neurons from the striatum, substantia nigra, septum, cerebral cortex, cerebellum, and dentate gyms. *J Neurosci Res* 42, 674-683.
- [0156] Briggs C A, McKenna D G, Piattoni-Kaplan M (1995) Human alpha 7 nicotinic acetylcholine receptor responses to novel ligands. *Neuropharmacology* 34, 583-590.
- [0157] Buccafusco J J, Shuster L C, Terry A V, Jr. (2007) Disconnection between activation and desensitization of autonomic nicotinic receptors by nicotine and cotinine. *Neurosci Lett.* 413, 68-71.
- [0158] Calhoun, Bosworth, Grambow, Dudley, & Beckham, (2002). Medical service utilization by veterans seeking help for posttraumatic stress disorder. *Am J Psychiatry*. 159 (12): 2081-6
- [0159] Chromy B A, Nowak R J, Lambert M P, Viola K L, Chang L, Velasco P T, Jones B W, Fernandez S J, Lacor P N, Horowitz P, Finch C E, Krafft G A, Klein W L (2003) Self-assembly of Abeta(1-42) into globular neurotoxins. *Biochemistry* 42, 12749-12760.
- [0160] Court J A, Johnson M, Religa D, Keverne J, Kalaria R, Jaros E, McKeith I G, Perry R, Naslund J, Perry E K (2005) Attenuation of Abeta deposition in the entorhinal cortex of normal elderly individuals associated with tobacco smoking. *Neuropathol Appl Neurobiol* 31, 522-535.
- [0161] Darden T A, York, D., and Pedersen, L. (1993) Particle mesh Ewald: An N.log(N) method for Ewald sums in large systems. *Journal of Chemical Physics* 98, 10089-10092.
- [0162] Daura X, van Gunsteren W F, Mark A E (1999) Folding-unfolding thermodynamics of a beta-heptapeptide from equilibrium simulations. *Proteins* 34, 269-280.
- [0163] Doolittle D J, Winegar R, Lee C K, Caldwell W S, Hayes A W, de Bethizy J D (1995) The genotoxic potential of nicotine and its major metabolites. *Mutat Res* 344, 95-102.
- [0164] Echeverria, V, Cuello, A C (2002) *Mol. Neurobiol.*, 26(2-3):299-316.
- [0165] Echeverria, V. et al. (2005) *Eur. J. Neurosci*, 22:2199-2206.
- [0166] Ferrer I, Marin C, Rey M J, Ribalta T, Goutan E, Blanco R, Tolosa E, Marti E (1999) BDNF and full-length and truncated TrkB expression in Alzheimer disease. Implications in therapeutic strategies. *J Neuropathol Exp Neurol* 58, 729-739.
- [0167] Gahring L C, Meyer E L, Rogers S W (2003) Nicotine-induced neuroprotection against N-methyl-D-aspartic acid or beta-amyloid peptide occur through independent mechanisms distinguished by pro-inflammatory cytokines. *J Neurochem* 87, 1125-1136.
- [0168] Gallinat J, Meisenzahl E, Jacobsen L K, Kalus P, Bierbrauer J, Kienast T, Witthaus H, Leopold K, Seifert F, Schubert F, Staedtgen M (2006) Smoking and structural brain deficits: a volumetric MR investigation. *Eur J Neurosci* 24, 1744-1750.
- [0169] Hammond D K, Bjercke R J, Langone J J, Strobel H W (1991) Metabolism of nicotine by rat liver cytochromes P-450. Assessment utilizing monoclonal antibodies to nicotine and cotinine. *Drug Metab Dispos* 19, 804-808.
- [0170] Hellstrom-Lindahl E, Court J, Keverne J, Svedberg M, Lee M, Marutle A, Thomas A, Perry E, Bednar I, Nordberg A (2004) Nicotine reduces A beta in the brain and cerebral vessels of APPsw mice. *Eur J Neurosci* 19, 2703-2710.
- [0171] Hess B, Bekker, H., Berendsen, H. J. C., and Fraaije, J. G. E. M (1997) LINCS: A linear constraint solver for molecular simulations. *Journal of Computational Chemistry* 18, 1463-1472.
- [0172] Hoge, C W et al., 2004, *N Eng J Med*, 351:13-22.
- [0173] Hong D P, Fink A L, Uversky V N (2009) Smoking and Parkinson's disease: does nicotine affect alpha-synuclein fibrillation? *Biochim Biophys Acta* 1794, 282-290.
- [0174] Hsiao K, Chapman P, Nilsen S, Eckman C, Harigaya Y, Younkin S, Yang F, Cole G (1996) Correlative memory deficits, Abeta elevation, and amyloid plaques in transgenic mice. *Science* 274, 99-102.
- [0175] Kabsch W, Sander C (1983) Dictionary of protein secondary structure: pattern recognition of hydrogen-bonded and geometrical features. *Biopolymers* 22, 2577-2637.
- [0176] Kessler (2000). Posttraumatic stress disorder: the burden to the individual and to society. *J Clin Psychiatr.* 61 Suppl 5 4-12; discussion 13-4
- [0177] Kessler et al., 2005, *Arch. Gen. Psychiatry*, 62:617-627.